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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,598	06/30/2006	Beth C. Mullin	UTR-108XC1	5764

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EXAMINER	
IBRAHIM, MEDINA AHMED	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,598	MULLIN ET AL.	
	Examiner	Art Unit	
	Medina A. Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/22/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Sequence a lignments*.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group III, 19-20 and 23-29 in the reply filed on 03/25/08 is acknowledged. Claims 1-24 are cancelled. New claims 25-76, drawn to an isolated polynucleotide, a vector, host cell, and plant comprising said polynucleotide, and plant transformation and phytoremediation methods are added.

Claims 25-76 are pending and are examined.

Sequence Listing

The sequence listing of 06/15/06 has been entered. However, the application does not comply with the sequence Rule §1.821 through 1.825 because the specification, on page 28 (paragraph 0089) recites sequences with no sequence identifier, SEQ ID NO. Also the sequences of claims 31, 33, 35, 43, 45, 47, 70, 72, and 74 lack SEQ ID NO: Nucleotide and /or amino acid sequences as used in §1.821 through 1.825 are interpreted to mean unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides in patent applications. The 37 CFR 1.821(d) requires the use of the assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is respectfully requested to identify the sequences in the specification on page 28, and in claims 31, 33, 35, 43, 45, 47, 70, 72, and 74, or to submit a new Sequence Listing, which comprises said sequences. The specification and claims should also be amended to recite SEQ ID NO:

Claim Objections

Claims 31, 33, 35, 43, 45, 47, 70, 72, and 74 are objected to for reciting sequence without a sequence identifier, SEQ ID NO:. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 20-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pawlowski et al (MPMI (1997), vol.10 (5), pp. 656-664; Applicant's IDS) in view of Sharma et al (US 5,594,115 A).

The claims are drawn to, *inter alia*, an isolated polynucleotide sequence encoding a multimeric polypeptide construct comprising (SEQ ID NO: 1)x, (SEQ ID NO: 4)x, [(L-SEQ ID NO: 1)]x, [(L-SEQ ID NO: 4)]x, or (SEQ ID NO: 1-(L)c)a-Lz-(SEQ ID NO: 4-(L)d)b]x; wherein x is an integer from 2 to 100; a, b can be the same or different and are integer from 1 to 50; c, d can be the same or different and are integer from 0 to 8, and z is an integer from 0 to 8; and wherein L is a linker, a peptide linker having specific amino acid residues and cleavable; an isolated host cell and a vector comprising said polynucleotide, said host cell comprising said polynucleotide sequence or a polynucleotide encoding SEQ ID NO: 3 fused to a heterologous sequence that chelates metal ion.

The specification teaches that SEQ ID NO: 1 is the full polypeptide sequence of AgNt84; SEQ ID NO: 3 is the signal peptide sequence of the polypeptide AgNt84; SEQ ID NO: 4 is the metal binding domain sequence of the polypeptide AgNt84; and SEQ ID NO: 2 is the cDNA (polynucleotide) encoding SEQ ID NO: 1, the polypeptide AgNt84 (pages 2-3 of the specification). Therefore, the sequences of SEQ ID NO: 3 and 4 are part of SEQ ID NO: 1.

Pawlowski et al teach an isolated cDNA encoding a glycine and histidine rich AgNt84 protein from Alnus glutinosa that is 100% identical to Applicant's SEQ ID NO: 1 (see attached alignment of sequences). Pawlowski et al also teach that the AgNt84 polypeptide contains a signal peptide having similarity with signal peptide from the nodule 24, the nodule specific protein from soybean. The cited reference teaches an E.coli host cell expressing the AgNt84 polypeptide encoded by the AgNt84 cDNA as

fusion protein with maltose binding protein. Pawlowski et al suggest that because the polypeptide encoded by AgNt84 cDNA without the signal peptide has the ability to bind to nickel resin it may function as a metal binding protein (see the whole document).

Pawlowski et al do not explicitly teach fusion or multimeric constructs of SEQ ID NO: 1, 3, or 4 or with linker peptides.

Sharma et al teach recombinant fusion proteins which comprise a metal chelating peptide which have at least six alternating histidine residues. At the paragraph bridging columns 2 and 2, Sharma cites US 5, 569,794 that teaches recombinant DNA encoding fusion protein containing metal chelating peptides, including those containing histidine, attached to a desired polypeptide via a linker peptide. At column 4, Sharma cites EPO 163573 that disclose DNA sequences encoding fusion polypeptides with cleavable linkers. Sharma et al also teach that the fusion protein is produced by host cells transformed with the genetic information encoding the fusion protein. The host cells may secrete the fusion protein into the culture media or store it in the cells whereby the cells must be collected and disrupted in order to extract the product (see the whole document).

Therefore, it would have been obvious to one of ordinary skill in the art to use the DNA construct comprising an isolated polynucleotide sequence encoding AgNt84 polypeptide taught by Pawlowski et al, and to modify that construct by incorporating two or more of the polynucleotide in a multimeric form separated by linker sequences to produce chimeric polynucleotides encoding fusion polypeptides separated by cleavable

linker peptides as taught by Sharma et al, to produce recombinant fusion proteins and purifying them with immobilized metal ions with a reasonable expectation of success as taught by Sharma et al. Applicant has not shown any unexpected result with the use of multiple polynucleotide sequences encoding SEQ ID NO: 1, 3 or 4 in the fusion construct. Since DNA sequences SEQ ID NO: 1, 3, and 4 are known in the prior art and as metal binding sequences as taught Pawlowski et al , one would have been motivated to use one or more of said sequences for production of recombinant protein in a host cell as taught by Pawlowski et al.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 52-76 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to, inter alia, a transformed plant comprising an isolated polynucleotide sequence encoding a multimeric polypeptide construct comprising (SEQ ID NO: 1)x, (SEQ ID NO: 4)x, [(L-SEQ ID NO: 1)]x, [(L-SEQ ID NO: 4)]x, or (SEQ ID NO: 1-(L)c)a-Lz-(SEQ ID NO: 4-(L)d)b]x; wherein x is an integer from 2 to 100; a, b can be the same or different and are integer from 1 to 50; c, d can be the same or different

and are integer from 0 to 8, and z is an integer from 0 to 8; and wherein L is a linker, a peptide linker having specific amino acid residues and cleavable; said transformed plant comprising a polynucleotide encoding SEQ ID NO: 4 or a polynucleotide encoding SEQ ID NO: 3 fused to a heterologous sequence that chelates metal ion; a method of using said transformed plant in phytoremediation of sites contaminated with metals.

The specification, however, does not provide guidance for a transformed plant expressing a polynucleotide encoding exemplified or non-exemplified polynucleotide sequence encoding the polypeptide sequence of SEQ ID NO: 1, 3, or 4 that is capable of phytoremediation of a contaminated site. It is also noted that SEQ ID NO: 4 is a metal binding domain; and SEQ ID NO: 3 is a signal peptide. Applicant ahs not disclosed a single transformed plant having a phytoremediation property as result of expressing a polynucleotide encoding SEQ ID NO: 4, or a polynucleotide encoding SEQ ID NO: 3 operably linked to a heterologous metal binding polypeptide. Therefore, the specification provides no more than an evitation to experiment, the claimed invention, requiring extensive and undue experimentation.

The ability of a plant to accumulate heavy metals is a genotype dependent and varies greatly between species and between cultivars within the species (Salt et al Biotechnology, vol. 13, pp. 468-474, 1995). Guerinot et al (Plant Physiology (2001), vol. 125, pp. 164-167) suggest that it is unlikely that the regulation of a single gene will be sufficient to convert non-metal accumulators into metal accumulators.

The state of the prior art as evidenced by Goldsbrough (1999, Phytoremdiation in a contaminated Soil and Water; CRC Press, Boca; pp. 221-2333) teaches

transformed Arabidopsis plants that didn't provide increased heavy metal accumulation as compared to control plants. Goldsbrough reports, "while ECS could restore some degree of Cd tolerance to a Cd-sensitive mutant (a cad2 mutant having reduced GSH levels), this gene didn't increase Cd tolerance of wild-type plants (page 230, 1st and 2nd full paragraphs).

Therefore, given the lack of guidance in the specification or in the prior art regarding a transformed plant capable of phytoremediation as result of expressing one or more of SEQ ID NO: 1, 3, or 4; the limited working example; the unpredictability in the art regarding the use of transgenic plants expressing a metal binding protein for metal accumulation/tolerance; the state of the art; and the nature of the invention as discussed above, the claimed invention is not enabled throughout the broad scope.

Applicant is invited to provide evidence in the form of a declaration under 37 CFR 1.132 to support the phytoremediation property of a transgenic plant expressing one or more polynucleotides encoding SEQ ID NO: 1, 3 or 4.

Remarks

No Claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571)272-0797. The examiner can normally be reached on M-TH 8:00 am to 5:30 PM, and every other Friday from 8:00 AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MAI
7/21/2008

/Medina A Ibrahim/
Primary Examiner, Art Unit 1638